REMARKS

The Amendment, filed in response to the Office Action mailed February 1, 2010, is believed to fully address all and every issue raised in the office Action. Favorable reconsideration on the merits and allowance of the application are respectfully requested.

Disposition of Claims and Amendment Summary

In the Office Action, claims 10-17 and 19-22 have been all the claims pending in the application and claims 10-17 and 19-22 have been rejected.

In the instant Amendment, new claim 23 is added. Support for claim 23 can be found by the disclosure of, for example, Examples 4, 9 and 11, in the specification. No new matter is introduced. Entry and consideration of the amendment are respectfully requested.

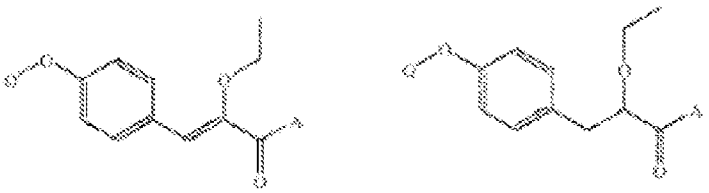
Withdrawn Rejection

Applicants thank the Examiner for withdrawing the previous rejection under 35 U.S.C. § 103 over Anderson in view of Nohira, in light of Applicants' arguments and amendments.

Response to Rejection of Claims 10-17 and 19-22

In the Office Action, claims 10-17 and 19-22 are rejected under 35 U.S.C. 103(a) as assertedly being unpatentable over Andersson et. al., US Patent No. 6,258,850, in view of Saburi et. al., US Patent No. 5,334,758.

Andersson is cited as teaching that compounds of formula (VII) can successfully undergo asymmetric hydrogenation to form compounds of formula (V).



(VII) (V)

Where A=OH; Q=H or a protecting group (column 4, lines 29-46; column 7, line 50-column 8, line 24). Andersson teaches that the asymmetric hydrogenation reaction is conducted in the presence of chiral transition metal catalysts such as Rh-BINAP, [EtDuPHOS-Rh(COD)], as well as a variety of other catalysts (column 8, lines 17-24).

The Examiner admits that Andersson fails to teach asymmetric hydrogenation in the presence of chiral ruthenium complexes such as Ru2C14[(S)-H8-binap]2NEt3 or Ru2C14[(R)-H8-binap]2NEt3.

Saburi is cited as teaching a process for preparing optically active carboxylic acids, through the asymmetric hydrogenation of α,β-unsaturated carboxylic acids with a chiral metal phosphine complex (Abstract). According to the Examiner, Saburi explicitly teaches that Ru_2C1_4[(S)-H_8-binap]$_2NEt_3$ or Ru_2C1_4[(R)-H_8-binap]$_2NEt_3$ are used to prepare optically active carboxylic acids (column 3, lines 41-43, and 56 and 58).

The Examiner concludes that one of ordinary skill in the art, at the time of the invention, would have been motivated to use the complexes Ru_2C1_4[(S)-H_8-binap]$_2NEt_3$ or Ru_2C1_4[(R)-H_8-binap]$_2NEt_3$ taught by Saburi for the asymmetric hydrogenation of the compounds of formula (VII) taught by Andersson, because Andersson teaches that such compounds can undergo

asymmetric hydrogenation with chiral rhodium complexes, and Saburi teaches that Ru_2C1_4[(S)-H_8-binap]$_2NEt_3$ or Ru_2C1_4[(R)-H_8-binap]$_2NEt_3$ are used to catalyze the hydrogenation of α,β -unsaturated carboxylic acids with high stereoselectivity. The Examiner further asserts that, as the compounds taught by Andersson are α,β -unsaturated carboxylic acids, one of ordinary skill in the art would have expected success in using complexes such as Ru_2C1_4[(S)-H_8-binap]$_2NEt_3$ or Ru_2C1_4[(R)-H_8-binap]$_2NEt_3$ catalyze the asymmetric hydrogenation.

Applicants' Arguments

Applicants respectfully traverse the rejection under 35 U.S.C. § 103 over Andersson in view of Saburi for the following reasons.

One skilled in the art would not have been motivated to use the catalysts of Saburi in an asymmetric hydrogenation using H_2 as a hydrogen donor.

Andersson was cited in the previous rejection as well and discussed in detail in Applicants' amendment submitted on December 11, 2009. Therefore, to the extent the discussion of Andersson and differences between Andersson and the claimed method of the instant application, Applicants' previous discussions are incorporated herein by reference, for the purpose of brevity.

Saburi teaches that catalysts other than Ru_2C1_4[(S)-H_8-binap]$_2NEt_3$ or Ru_2C1_4[(R)-H_8-binap]$_2NEt_3$ are also used to prepare optically active carboxylic acids.

However, Saburi's method requires a use of an excessive amount of an alcohol as a hydrogen donor (column 1, lines 38-61; column 2, lines 45-63) and teaches away from using H_2 as a hydrogen donor (comparative example 1, Table 3 on column 6).

Therefore, one skilled in the art would not have been motivated to combine the teaching of Andersson with the teaching of Saburi, and would have taught away from using H2 as hydrogen donor when the chiral Ru catalysts of Saburi is used in asymmetric hydrogenation.

Accordingly, Applicants believe that the rejection under 35 U.S.C. § 103 over Andersson in view of Saburi is not sustainable, and withdrawal of the rejection is respectfully requested.

In addition, Applicants respectfully disagree with the Examiner's position and understanding of Chen (Angewandte Chem., 46, pp. 4141-44, 2007) (submitted on December 11, 2010 as evidence supportive of Applicants' arguments). The Examiner asserts that Chen teaches on p. 4143, Table 2 an asymmetric hydrogenation of α-alkoxy cinnamic acids with chiral rhodium complexes, with high % ee values, and thus, these references do not discredit the teachings of Andersson. Office Action, pages 3-4, paragraph 3. However, as discussed below, Chen clearly reports that enantioselective hydrogenation of α-substituted cinnamic acid was very challenging and difficult when the instant application was filed in 2003.

State of the art when the invention was made – asymmetric hydrogenation of α-substituted cinnamic acids remains a challenge

When the invention defined in the claims of the instant application was made, i.e., in or about 2003 (the priority date of the instant application is November 27, 2003), the enantioselective hydrogenation of α-substituted cinnamic acids remains a challenge, as Chen expressly reports. On page 4142, left column, lines 4-1 from the bottom, Chen reports "Nowadays (Note – Chen was published in 2007 and thus this "nowadays" is understood to be in or around 2007), significant progress has been achieved in asymmetric hydrogenation of a wide

range of unsaturated substrates, but the enantioselective hydrogenation of α-substituted cinnamic acids remains a challenge."

Long-felt need, but unsolved problem

Chen also reports "Chiral α-substituted dihydrocinnamic acid derivatives are key intermediates in the synthesis of several bioactive compounds …" (page 4142, left column, lines 9-5 from the bottom) and "Recently, the synthesis of optically enriched α-alkoxydihydrocinnamic acids has attracted significant attention" (page 4142, right column, lines 19-16 from the bottom). Therefore, it can be understood that asymmetric hydrogenation which can effectively obtain high optical purity has been needed.

In addition, Chen states "The Rh-catalyzed enantioselective hydrogenation of 3-aryl-2-ethoxyacrylic acids is usually extremely difficult." (page 4142, right column, lines 13-11 from the bottom.)

That is, at the filing date of the present application, there was a need for an effective asymmetric hydrogenation of α-substituted cinnamic acid," which is a key intermediate of several bioactive compound, but one skilled in the art has recognized that it was extremely difficult to succeed in asymmetric hydrogenation of α-alkoxycinnamic acids.

Chen, in particular, explains in the paragraph bridging page 4142, right column to page 4143, left column, the mechanism of asymmetric hydrogenation which was generally recognized in the art and reports "Unlike enamides, enol acetates, and itaconates, α-substituted cinnamic acids lack such functionality at the β position to coordinate with the metal,and so most known chiral diphophine ligands give low enantioselectivities and activitires for the Rh catalyzed asymmetric hydrogenation of α-substituted cinnamic acids."

Applicants note that the Examiner asserts that Chen teaches the asymmetric hydrogenation of a-alkoxy cinnamic acids with chiral rhodium complexes, with high % ee values, and, therefore, these references do not discredit the teachings of Andersson et. al. in view of Norah. Applicants respectfully submit that the high % ee values obtained by Chen in or around 2007 is attributed to the use of TriFer (a new ferrocene-based C2-symmetric diphosphine ligand), of which structure is depicted on page 4141, right column, Scheme 1. The enantioselective hydrogenation employed by Chen is different from the reaction defined in the claims of the instant application and it does not provide any basis for discrediting the teachings of Andersson.

Chen clearly shows that, when the invention defined in the claims of the instant application was made in or around 2003, an effective enantioselective hydrogenation of α-substituted cinnamic acid was desired, but it was extremely difficult to attain the goal.

This is further supported by a copy of CHEMICAL & ENGINEERING NEWS, published October 27, 2003, which shows that there was still a need for a method for successfully synthesizing a compound (on the left box) that corresponds to a compound of formula (6) of the present invention, by providing a reward for such a successful synthesis. Therefore, when the instant application was filed, it was recognized that it was not obvious to prepare this compound.

Applicants submit a copy of CHEMICAL & ENGINEERING NEWS (1 page) in a separate cover. In this regard, it is respectfully submitted that no IDS is required for the consideration of the publication, because this publication is submitted in support of Applicants' argument made in response to the Examiner's rejection. MPEP 609.

In conclusion, contrary to the Examiner's assertion that Andersson et. al. teaches that a asymmetric hydrogenation can be successfully performed on compounds such as those instantly

claimed, with chiral rhodium complexes and other metal catalysts, those skilled in the art would not have recognized that a asymmetric hydrogenation can be successfully performed on compounds such as those instantly claimed, with chiral rhodium complexes and other metal catalysts.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number **202-775-7588**.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

/Sunhee Lee/

Sunhee Lee
Registration No. 53,892

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

WASHINGTON OFFICE
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CUSTOMER NUMBER

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